PRIMARY TUMORS OF THE URINARY BLADDER.

A STUDY OF FORTY-ONE CASES AT THE MASSACHUSETTS GENERAL HOSPITAL.*

BY LINCOLN DAVIS, M.D.,

OF BOSTON, MASS.,

Out-Patient Surgeon, Massachusetts General Hospital; Instructor in Anatomy, Harvard Medical School.

THE cases which form the basis of this paper are taken from the clinical records of the Massachusetts General Hospital since 1877, and the autopsy records since 1897. There are included in this series of forty-one cases only primary tumors of the bladder which have been verified by either operation or autopsy. Many cases in which the diagnosis was made by the presence of villous fragments in the urine, or from clinical symptoms, or by the cystoscope, but which for various reasons did not come either to operation or autopsy, are not included. Neither are numerous cases of malignant disease of the bladder, obviously secondary to cancer of the uterus, prostate, or intestines, included.

The object of this study has been:

First. To record such clinical data, as the analysis of a considerable number of cases affords, with special reference to end results after operation.

Second. To investigate the pathological anatomy of the simple epithelial tumors of the bladder, commonly called papillomata, with relation to the ultimate prognosis.

To this purpose the hospital records have been carefully analyzed, and after persistent search, reliable information as to the histories of patients after discharge from the hospital have been pretty generally obtained; personal interviews were possible in a few cases. All the pathological specimens which were preserved have been reëxamined, and studied in relation to each other, and to the clinical course of the disease.

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In thirty-seven of the forty-one cases included in this report, the tumors were removed by operation; in the remaining four cases the condition was found at autopsy. A summary of the cases in the form of a table follows at the end of this article.

ETIOLOGY.

Prevalence.—The fact that in the twenty-eight years since 1877 only thirty-seven cases of primary tumors of the bladder have been operated upon at this hospital, leads one to believe that the disease is a comparatively rare one, at least in this locality.

It is interesting to note that in the same period of time there have been four hundred and forty-two cases of stone in the bladder operated upon. This comparison, however, is not strictly fair, for it is reasonable to suppose that a greater number of cases of tumor than of stone have been overlooked, since the diagnosis of the former condition was, until the perfection of the cystoscope within recent years, rather uncertain, while a perfectly adequate method of diagnosticating stone has been known for years. Then, too, doubtless in the earlier years, on account of the greater formidableness of the operation for tumor as compared to that for stone, some of the former cases even if diagnosticated may not have been attacked.

By decades the cases of tumor group themselves as follows: 1877–1887, 5 cases operated on; 1887–1897, 14 cases operated on; 1897–1905, 18 cases operated on. The increase since 1897 is not striking, considering the improved methods of diagnosis and operative technique.

That the disease is generally considered a rare one is shown by the much-quoted figures of Küster, who found 10 cases out of a total of 3938 cases of tumors of all kinds operated upon at the Augusta Hospital in Berlin, ¼ of 1 per cent. Gurlt collected 66 cases out of 16,637 cases of tumors in 3 large hospitals in Vienna, less than 0.4 per cent.

Albarran, on the other hand, maintains that tumors of the bladder are far from rare, and cites the fact that in Guyon's ward at Necker in 4 years there were 55 vesical tumors, or 3.9 per cent. of all genito-urinary cases there treated.

Sex.—In this series of cases there were 7 females and 34 males, an excess of males slightly less than that reported in other collections of cases. Albarran's figures are 14 per cent. of females in 381 cases. Nitze's figures show a still smaller percentage of females.

Age.—The age at which the patients entered the hospital with the disease has been noted. In decades the cases group themselves as follows: Under 20 years, 1 case; 20–30, 2 cases; 30–40, 2 cases; 40–50, 5 cases; 50–60, 21 cases; 60–70, 7 cases; 70–80, 8 cases. This shows a marked preponderance of cases in the sixth decade, a fact generally noted. The youngest patient was 16 years old, a case of sarcoma; the oldest 73. The average age was 53.

Excluding two comparatively rare forms, myxoma and sarcoma, which occur in childhood, the first exclusively and the second commonly, tumors of the bladder in general, although occurring throughout adult life may be said to essentially belong to the period of middle life, and early old age.

Cause.—The direct cause of tumors of the bladder as of tumors elsewhere in the body is not known. The frequency with which certain cell inclusions have been found in the epithelial tumors of the bladder, has led to considerable discussion of the parasitic theory in connection with their origin.

According to the weight of best authority, however, these cell inclusions can be adequately explained as the products of either cell activity or degeneration, as the case may be, and the parasite remains to be actually demonstrated.

Of predisposing causes several have been advanced from time to time and seem to have more or less weight. Chief of these is irritation (chemical, mechanical, or bacterial).

That chemical irritation of the bladder has some relation to the formation of bladder tumors seems to be borne out by the prevalence of this condition among workers in aniline factories. A striking number of such cases have been reported by Rehn, Leichtenstern, and Huldschiner. It cannot be doubted, it seems to me, that there is here something more than mere coincidence. That it is more than a contributing factor, however, cannot be claimed in view of the small proportion of cases to which it applies relative to the total number of bladder tumors.

In this series of cases chemical irritation of the bladder seemed to play no part in the causation of the disease, so far as an investigation of the occupations of the patients could determine this point. The occupations were various, and diverse, including all the ordinary vocations of life; sea-faring men, of whom there were five, were for some unaccountable reason in the majority.

The mechanical irritation of stone in the bladder has been considered an etiological factor of importance. Rosenow has collected from the literature 44 cases in which stone was associated with tumor. From a study of the clinical history and post-mortem findings of these cases, he reasons that the stone was primary in 18 cases, and the tumor in 8. He concludes "that contrary to the views of Neelsen, Busse, and others, an etiological relationship between calculus and tumor is not to be denied altogether, and calculus seems to favor the development of tumor in a larger percentage of cases than tumor favors the development of stone."

The latter part of this conclusion is not only contrary to the views of the authors quoted above, but is at variance with the opinions of such authorities as Guyon, Albarran, and Nitze. The former says that it can be affirmed that preceding diseases of that organ (the bladder) or of the urethra, such as gonorrhœa, stricture, cystitis, stone, retention, hypertrophy of the prostate predispose to tumors of the bladder in no way. Nitze makes a statement to the same effect.

Furthermore, there is considerable evidence that tumor does favor the development of stone in many cases, the secondary changes in the bladder which inevitably sooner or later result from the presence of a tumor, such as inflammation, ulceration, retention, etc., furnishing the very conditions which are most favorable for the formation of a calculus.

The well-known frequency of calcareous incrustation of tumors is evidence of this tendency. It is merely a further step in the same process to the formation of a true calculus about a detached fragment of tumor, and such cases have been reported.

An investigation of cases in this hospital with reference to the association of stone and tumor may be of interest. It is a striking fact that of the 438 individuals who underwent 492 operations for stone in the bladder since 1872, only one (Case XVIII) according to the records, subsequently developed a tumor of the bladder. If others did so the condition was either unrecognized, or treated elsewhere. Among this number there were many cases of recurrent vesical calculi with repeated operations, which were doubtless subjected to the "irritation of stone" in no small degree. It must in fairness be said, however, that in a number of these cases of recurrent vesical calculi there was enlargement of the prostate gland, and that in at least one of them, possibly more, it was afterwards discovered that the gland was carcinomatous. Such cases not being primary tumors of the bladder, are not included in this series, but are mentioned as possibly throwing some light on the difference of opinion which exists as to the association of stone and tumor.

Of the forty-one cases of primary tumors of the bladder, in addition to Case XVIII, already mentioned, there were 7 cases in which there was an association either past or present with true calculus or deposition of urinary salts.

These cases, Nos. I, IV, XV, XVIII, XXIII, XXIX, XXXI, and XXXVI, may be briefly summarized as follows:

CASE I.—A villous tumor of the bladder incrusted with urinary salts was removed by Dr. Warren. No history of previous stone. Death 14 years later. Cause of death recorded in Massachusetts Archives as "renal calculi."

CASE IV.—Service of Dr. Bigelow. Urinary symptoms for 8 months, with hæmaturia for 2 months. At operation a lithotrite was introduced into the bladder and what seemed to be a soft stone seized and crushed. The evacuator brought out some fragments of stone with blood-clots. A vaginal cystotomy was then done, and a tumor the size of two English walnuts removed from the bladder. The patient died at the end of 7 days.

CASE XV.—This case has been reported in detail by Dr. A. T. Cabot.[1] A brief résumé follows here:

In 1870, in another city, the patient was cut for stone by the lateral perineal route. Frequency of micturition persisted ever after this. In 1884 there was a sharp attack of cystitis, and five years later fragments of stone were passed. In September, 1889, the patient entered the hospital; the bladder was searched for stone, washed out with the Bigelow evacuator, and several small fragments composed of papillary masses of epithelial cells mixed with urinary salts came away. Suprapubic cystotomy was then performed by Dr. Cabot, and a thick, flat, cutaneous-looking sheet of tissue removed from surface of bladder,—"Pachydermia vesicæ."

In March, 1892, the patient began to have pain in the bladder and frequent micturition again. In July, 1894, he reëntered the hospital with a discharging sinus above the pubes. The sinus was enlarged by Dr. Cabot and the interior of the bladder explored: it was found invaded by a new growth. A small portion which was removed proved to be epidermoid cancer. The patient died a short while later, and at autopsy the bladder, as well as the kidneys, muscles of abdominal wall and retroperitoneal glands, were found to be involved in the disease.

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[1] Papers on Genito-Urinary Surgery. "A case of cystitis with formation of a thick epidermal sheet in the bladder,—Pachydermia vesicæ."

CASE XVIII.—This case also has been reported by Cabot[2] There was a history of stricture of the urethra, for which no operation was done. Six years later, after an attack of renal colic (?), a few small, pea-sized stones were passed. Eight years later, symptoms of cystitis developed, which steadily increased for a year, until a small stone in the bladder was crushed by Dr. Cabot in 1895. In the course of a few months there were two recurrences of stone, for which there was no apparent cause, as the bladder emptied itself and the urine was acid. In November, 1895, the bladder was opened above the pubes by Dr. Cabot; a stone was removed from the postprostatic pouch, and a little myoma with ulcerated, granulating surface, incrusted with urinary salts was removed. There was no recurrence of symptoms for 2 years. History after this time not known.

CASE XXIII.—Service of Dr. Elliot. Symptoms of cystitis with hæmaturia following confinement 2 years before. Passed several small stones during the preceding year. In May, 1900, the urethra was dilated and two small tumors removed from bladder. In December of the same year she reëntered the hospital with the same symptoms, and a history of having passed blood and some stones. A suprapubic cystotomy was done by Dr. Greenough. A deposit of calcareous matter was curetted off the bladder wall, and two papillomatous masses removed. No history subsequent to the discharge from the hospital could be obtained.

CASE XXIX.—Hæmaturia of 3 months' duration. Papillary tumor incrusted with urinary salts removed by suprapubic cystotomy by Dr. Cabot. No urinary symptoms 2 years later.

CASE XXXI.—Operation 31 years ago at the age of 9 for stone in the bladder. No urinary symptoms from that time until the beginning of the present trouble, 3½ years ago, when he first noticed bloody urine which has persisted intermittently since. In February, 1904, a papillary tumor of the bladder was removed by Dr. Cabot. No stone. In August of the same year he returned to the hospital with recurrence of symptoms. The bladder was reopened by Dr. Conant and found studded with nodular growths, which were curetted out and cauterized. He left the hospital somewhat relieved. Death from the disease ensued two months later.

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[2] Papers on Genito-Urinary Surgery. "Observations upon stone in the bladder."

CASE XXXVI.—A large fibro-myo-sarcoma removed by Dr. Balch, the lower portion of the growth was incrusted with urinary salts.

Of these 8 cases there were 4 (Cases I, IV, XXIX, and XXXVI in which there was not true stone formation, but incrustation of existing tumors with urinary salts. In these it is evident that the tumor was the primary factor.

In 2 cases (Nos. XVIII and XXIII) it is not possible to determine which was the primary etiological factor. In Case XVIII, the probability of the early stones having favored the development of the tumor, a myoma, is at least offset by the contrary evidence that the late ones were the result of it. Case XXIII is inconclusive through incompleteness of subsequent history.

Two cases (Nos. XV and XXXI) in which the stone was unquestionably primary in point of time, remain to be considered. Case XV was complicated by the rare condition of pachydermia vesicæ, which is of notoriously slow development, and therefore very likely may have antedated both conditions, the persistence of the bladder-symptoms after removal of the stone giving color to this view. Be that as it may, there are at least as good grounds for attributing the tumor, which was epidermoid cancer in this case, to a malignant transformation of the leukoplakia, as to the direct result of a single stone removed 24 years previously.

Hallé, who reported 7 personal cases of leukoplakia of the bladder, in 1896, advanced the theory of the malignant degeneration of this condition. He supported his theory on the evidence of one of his own cases, in which the coexistent lesions of leukoplakia and cancroid were found, and also on the analogy of a similar tendency in leukoplakia of the mouth.

Of Hallé's 7 cases it is interesting to note that 4 were associated with stone; in 3 of these the stone was evidently secondary in origin, in the fourth case this point could not be determined.

CASE XXXI.—There can be no question but that the calculus was primary in this case, the interval of 26 years, however, between the removal of the stone and the onset of tumor symptoms,—an interval characterized by the entire absence of all bladder symptoms,—makes it hard to believe that "irritation" played an important part in the causation of the tumor.

Among these cases should be mentioned for the sake of completeness 2 cases (Nos. XXXII and XXXVIII) in which the patients gave a history of having passed gravel, respectively, 1 and 2 years previous to entrance to the hospital. In neither of these cases was stone or deposition of urinary salts found in the bladder. The unconfirmed observation of a patient as to the passing of gravel is liable to too many sources of error to be accepted without scepticism, and therefore it seems not worth while to consider these 2 cases further.

As far then as an analysis of these cases goes, it may at least be said that no strength is added thereby to the irritation-of-stone theory.

Under the head of mechanical irritation should be mentioned the effects of the distoma hæmatobium. The occasional association of papilloma, carcinoma and sarcoma with Bilharzia disease of the bladder has been reported by Goebel. Zuckerhandl, in his "Handbuch der Urologie," pictures very beautifully a "Bilharzia papillom" showing numerous calcified distoma embryos in the stroma of the tumor. This source of irritation, like the aniline poisoning, is of great interest, but is necessarily restricted to a very limited field and lies outside the scope of this paper.

Bacterial irritation of the bladder as in cystitis, enlarged prostate, etc., may be dismissed as of no real importance in the causation of bladder-tumors, except possibly in the rare instances of epidermoid cancer. In only a small proportion of cases in this series was there any history of urinary disturbance antedating the symptoms which could be properly ascribed to the tumor itself.

Early gonorrhœa had been present in 6 cases. No sequelæ of that disease were mentioned in the histories except in one case, where stricture of the urethra had been present 15 years previous to the tumor.

In 16 cases it was stated that there never had been gonorrhœa. In 19 cases there were no data as to this point.

Symptoms of cystitis,—that is, frequent and painful urination,—were the first complaints in 15 cases, but the cardinal symptoms of tumor, hæmaturia, followed shortly in all; the only exceptions being Case XVII in which there was a period of 5 years characterized by frequency of micturition and scalding before the onset of hæmaturia; Case XVIII, a myoma, in which hæmaturia was never noted; and Case XL, in which there had been recurrent attacks of pain in the left kidney region for 20 years preceding the occurrence of blood in the urine.

The cases in which there was a previous history of stone have already been detailed.

In the remaining 20 cases hæmaturia was the first urinary symptom noted.

PATHOLOGY

In 28 of the total of 41 cases, microscopical examination of the tumors removed were recorded. According to these reports there were 15 cases of cancer, 10 of papilloma, 2 of sarcoma, and 1 of myoma. Under the first heading were included such varieties as infiltrating cancer, epithelioma, villous and papillary carcinoma, adeno-carcinoma, mesothelial cancer, and epidermoid cancer. Under the heading "Papilloma" were included 4 cases designated as malignant papilloma, one case as probably malignant, and 2 cases in which the question of malignancy could not be determined from the specimen. Of the 2 sarcomata, one was a round-cell variety, the other a fibro-myo-sarcoma. There were 3 cases in which secondary operations were done for recurrent tumors; in one case the recurrent growth was reported to be of the same nature as the original,—viz., cancer; in another a papillary cancer was reported to have recurred as a papilloma, and in a third an epithelioma as a carcinoma.

To the multiplicity of terms employed by different investigators with regard to the epithelial tumors of the bladder, are to be attributed seeming discrepancies, which are more apparent than real, but which are nevertheless confusing.

How shall a malignant papilloma be distinguished from a papillary cancer, or an epithelioma from a papilloma, or carcinoma?

Recourse to the literature does not dispel this confusion, as a most varied nomenclature and classification of these growths has been adopted by different authorities. With the hope of clearing away the confusion on this subject in my own mind at least, a careful study has been made of the pathological specimens which had been preserved in 19 cases, and were kindly placed at my disposal.

Classification.—It seemed necessary at the outset to adopt a classification for these tumors. That proposed by Küster, based on histological structure, dividing tumors of the bladder into 3 groups according to the 3 elements of the bladder-wall, —epithelial, connective tissue, or muscular,—from which their principal elements are derived, is the simplest and perhaps the most generally accepted. This has been followed with one radical change in interpretation for which there is good authority, namely, the transposition of the papilloma (Zottenpolyp of Küster) from group 2 to group 1. With this change the classification stands as follows:

1. Epithelial group	papilloma carcinoma adenoma cysts
2. Connective-tissue group	sarcoma myxoma fiibroma angioma
3. Muscle group	myoma

This is essentially the classification of Albarran reduced to its simplest terms. It does not include certain rare forms of bladder tumors such as rhabdo-myoma, chondroma, and dermoids, which are not derived from any normal elements of the bladder-wall, and for which Albarran makes another class under the name "Heterotopic." As none of these rare forms was observed they are mentioned only to be dismissed from further consideration.

Papilloma.—The term "papilloma" has been retained in this classification, objections on the score of ambiguity of the word being outweighed by the sanction of long usage in English medical literature. The term as here used refers to a pedunculated papillary or villous tumor consisting of a branching connective-tissue stalk, containing blood-vessels and occasionally smooth muscle-fibres, covered with one or more layers of epithelial cells, but without epithelial infiltration of the bladder-wall. This tumor is classed under the first or epithelial group, as the epithelial element in it is regarded as the essential one. There are, however, great variations in the proportions of epithelium and connective tissue in different specimens. All gradations occur from the tumor in which the connective tissue forms a thick and massive stalk with but a thin covering of two or three layers of epithelial cells, a form which is hardly to be differentiated from the pure fibroma, to that in which the connective tissue is reduced to a mere line threading its way brokenly between masses of epithelial cells packed in countless layers.

Yet in the main two types of papilloma stand out as fairly distinct, the villous and the lobulated. The villous type, "fimbriated papilloma" of Sir Henry Thompson, is characterized by the delicacy and tenuity of its connective-tissue processes, which spring like a tuft of grass from a circumscribed base. The structure of the tumor is so delicate that it collapses into a soft mass when exposed to the air, and it is only when observed in a fluid medium that its slender filamentous nature is appreciated. Microscopically the epithelial covering is usually comparatively thin, comprising but a few layers of cylindrical cells. By some observers this variety is regarded as merely an early stage in the development of the second type, the lobulated papilloma, "fibro-papilloma," of Thompson. In the lobulated papilloma the connective-tissue stalk is thicker and more branching, and the epithelial covering also, as a rule, considerably thicker, so that the tumor has a firmer consistency and retains its shape when removed, resembling closely a miniature cauliflower.

There may also be marked divergence from the normal type on the part of the epithelial cells in these tumors, as to size, shape, and arrangement, so that some of these papillomata may present most atypical or malignant aspects, so-called transitional forms, which are only to be differentiated from the true carcinoma by the absence of epithelial invasion of the bladder-wall.

There being then such variations in the structure of this form of tumor, it is but natural that there should have been much confusion as to its terminology and classification. The terms, "fungus" of early authors, "zottenkrebs" of Rokitansky, "Fibroma papillare" of Virchow, "papillary epithelioma" of Zeigler, "zottenpolyp" of Küster, "fimbriated" and "fibro-papilloma" of Thompson, and "villous tumor" of many writers, all refer to this same growth, and illustrate well enough the different points of view from which it has been regarded. Nitze, though retaining the term papilloma, follows Virchow and Küster in classifying it as a connective-tissue tumor.

Carcinoma.—There is corresponding confusion on the subject of primary carcinoma of the bladder, particularly in regard to that form commonly called papillary or villous carcinoma, which is generally conceded to be the most prevalent variety. There has been and still is great divergence of opinion among authorities as to what constitutes a papillary carcinoma of the bladder. Rokitansky held that all papillary epithelial tumors of the bladder were malignant, and designated them as zottenkrebs. This view is still held to a certain extent. Virchow was the first to emphasize the fact that benign "papillary fibromas" did occur. The existence of benign epithelial tumors of the bladder has been amply confirmed since.

Albarran distinguishes two forms of epithelial tumors of the bladder according to the type of their epithelial coverings, —the benign papillomata, or (as he prefers to call them) "polyps bénins," and the malignant epitheliomata. If the type of the normal epithelial cells of the bladder is reproduced, then the tumor is a papilloma; if the cells are, on the other hand, atypical, then the growth is an epithelioma.

Other authorities, notably Orth and Ziegler, make epithelial infiltration of the bladder-wall, and the formation of metastases, the distinctive sign of a carcinoma in this locality as elsewhere.

The fact, which is pretty generally recognized, that a benign papilloma may undergo carcinomatous degeneration, makes it evident that there must be a stage in this process when it will be exceedingly difficult, if not impossible, to determine whether a growth is benign or malignant; the term "transitional" has been applied in such cases. This tendency of papillomata to malignant degeneration will be considered in more detail later.

It is also a generally-conceded fact that of two tumors which are otherwise macroscopically and microscopically indistinguishable, the bladder-wall may show epithelial infiltration in one, and not in the other.

Under these circumstances it seems requisite for the sake of clearness and uniformity in differentiating these papillary growths, that the condition of the underlying bladder-wall in regard to epithelial infiltration should be made the crucial test of malignancy, rather than the character and arrangement of the cells in the growth itself. The former criterion is definite and precise, and even if its application is not possible in all cases of operative removal of the tumors, is, nevertheless, to be preferred to one which, although possessing a wider range of application, is so indefinite and subtle, and subject to such latitude of personal interpretation, as to surely lead to differences of opinion.

Other forms of carcinoma, such as the diffuse or nodular infiltrating growths, are distinctive and offer no difficulties in recognition.

Relative Frequency of Papilloma and Carcinoma.—As the result of differences of definition among authorities, there are widely divergent views as to the relative frequency of papilloma and carcinoma.

Albarran may be quoted as an exponent of the view that malignant growths greatly predominate. He records 81 epithelial tumors of the bladder which were histologically studied by himself. Of these, 13 in which the epithelium was considered typical, were classed as papillomata, and 68 in which it was atypical, were classed as epitheliomata, without reference to the question of infiltration of the bladder-wall. The word epithelioma is here used, according to the custom in France, as indicative of malignancy.

Nitze, who upholds the contrary view, mentions 220 cases of his own which were anatomically studied. Of these 144 were papillomata, 64 carcinomata, 2 adenomata, 7 sarcomata, and 5 myxomata.

Küster was the first to point out a source of error which doubtless led many observers to consider as malignant, papillary tumors which were really benign. This was the appearance of masses of epithelial cells surrounded by a connective-tissue framework which might give at first the impression of alveolar carcinoma, but which a closer study, especially of serial sections, revealed as folds between the papillary processes, cut in such a manner as to produce this effect. Another source of error which has been pointed out by Colley is the possibility of fragments of epithelial cells broken from the delicate villi of the tumor in the process of preparing the section, becoming transposed to other portions of the section, where they may be regarded as evidences of metastases. I have frequently observed little clumps of epithelial cells scattered about the edges of the tumor, at the base, as well as on the surface, which I have regarded as due to this cause.

With this preliminary clearing of the path, we may proceed to a consideration of the cases in hand.

Analysis of Cases.—Specimens were personally examined in 19 cases; of these 17 belonged to the epithelial group, with which this analysis is particularly concerned.

In 6 of these 17 cases there was satisfactory evidence, either microscopical or macroscopical or both, of epithelial invasion of the bladder-wall. These cases were, therefore, regarded as carcinomata.

In 7 cases the specimens allowed of a more or less complete examination of the underlying bladder-wall, which was found to be free from epithelial infiltration. These cases were, therefore regarded as papillomata.

In the 4 remaining cases the specimens did not contain any portion of the bladder-wall. So that the question of epithelial infiltration could not be determined by the microscope in them. Neither was there macroscopical evidence of infiltration at the time of operation. These cases must be considered doubtful, then, as far as this test goes. It is in such cases that the structure of the tumor itself, and particularly the type and arrangement of the epithelial cells, offer a clue of more or less value as to the benign or malignant nature of the growths. On these grounds, which have already been characterized as unsatisfactory, these 4 cases have been tentatively classed among the papillomata.

Cases of Papilloma.—The specimens in the 4 doubtful cases (Nos. XX, XXI, XXVI, XXXV) may be briefly described as follows:

CASE XX.—The specimen in this case was a papillary growth the size of a chestnut, which on section showed a pedicle, without bladder-wall, from which sprung a rather coarse, branching, vascular, connective-tissue framework, markedly infiltrated with round cells and covered by a many-layered epithelium of fairly regular type, and not excessive thickness. The line of demarcation between epithelium and connective tissue was fairly sharp. No mitoses were observed.

CASE XXI.—The specimen, one of two similar ones removed, consisted of a papillary growth of about the same size as the preceding one, showing none of the bladder-wall. The branching connective-tissue stroma was slight and exceedingly vascular. The epithelial covering was of considerable thickness in places, and here and there were clusters of epithelial cells in a concentric arrangement forming epithelial whorls. Line of demarcation not everywhere sharp; no mitoses. (See Figs. 4 and 5.)

CASE XXVI.—The section was of a papillary growth, somewhat larger than the two preceding, showing a number of branching stalks springing separately from a common base, composed of connective tissue without muscle-fibres. The papillary processes consisted of a central branching stalk of connective tissue of some thickness, containing blood-vessels clothed with a many-layered epithelium which, for the most part, did not greatly exceed in thickness the width of the stalk. The epithelial cells were of large size and quite uniform, cylindrical at the base, becoming cuboidal at the surface, disposed in layers, 12 to 30 in number, approximately. They presented a regular and typical arrangement. Mitoses were however, strikingly numerous. The line of demarcation between epithelium and connective tissue was particularly clear cut. There was some small cell infiltration of connective tissue of base and a number of plasma cells. (Fig. 6 and 7.)

CASE XXXV.—Sections consisted of fragments of a papillary tumor the size of a pigeon's egg (Fig. 1), showing neither base nor bladder-wall. The delicate connective-tissue stroma was covered with a many-layered epithelium of very considerable thickness. The cells were of fairly large size and were so closely packed together in places as to partially obliterate the spaces between neighboring papillary processes. Occasional mitoses were observed. The line of demarcation between epithelium and connective tissue was sharp.

In the sections of all these cases there were masses of epithelial cells entirely surrounded by a connective-tissue stroma; these are all, however, susceptible of Küster's explanation. In Cases XX and XXVI there were small clumps of epithelial cells scattered about the edges of the specimens, at the base as well as at the surface; these were considered to be the result of trauma to the specimen after its removal.

It would surely be difficult to draw accurate differential conclusions as to their benign or malignant character from the histology of these specimens. Of the four, No. XXVI, except for the number of mitoses, showed the most typical epithelium.

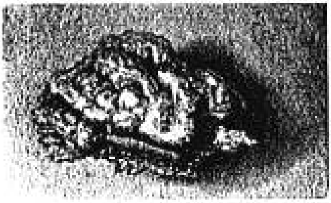

Fig. 1. Lobulated papilloma natural size (Case XXXV).

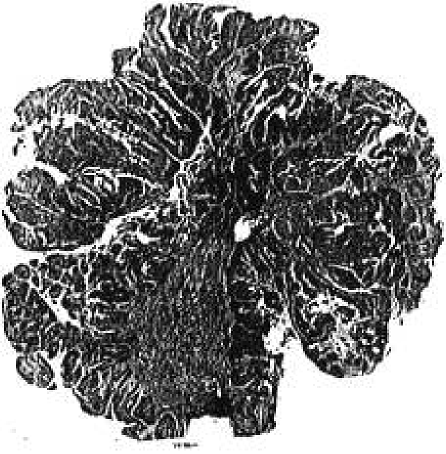

Fig. 2. Section of a lobulated papilloma x 4 diameters (Case XXXVII).

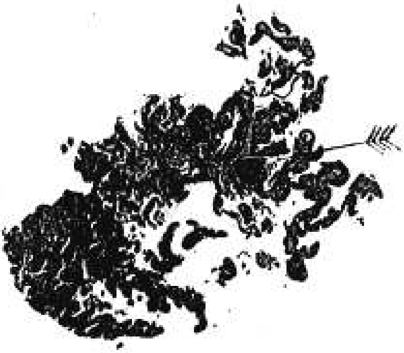

Fig. 4. Section of lobulated papilloma x 5 diameters (Case XXI). This was a recurrent growth removed 8 years ago, with no subsequent recurrence.

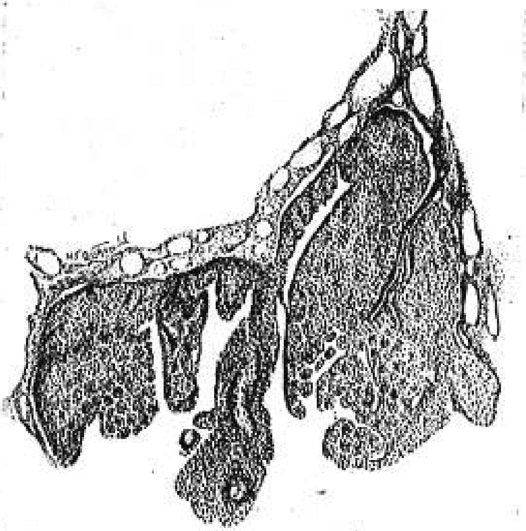

Fig. 5. Low-power drawing of detail of same at point marked by arrow. Shows vascularity of connective tissue stalk, and comparative thickness of epithelial covering, which has been drawn on one side of the stalk only. The concentric arrangement of the epithelial cells in small clusters is quite striking.

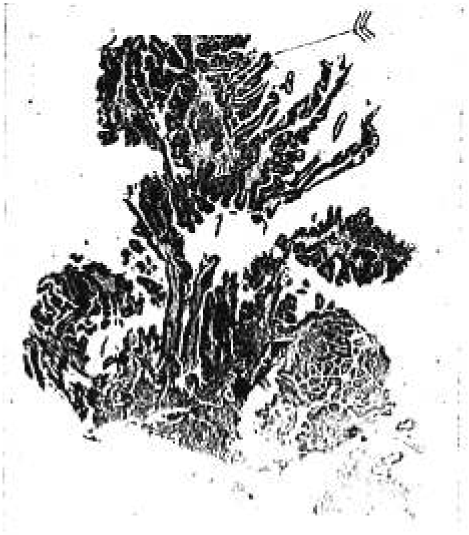

Fig. 6. Section of papillary epithelial tumor x 5 diameters (Case XXVI). In this case there was recurrence with death from the disease.

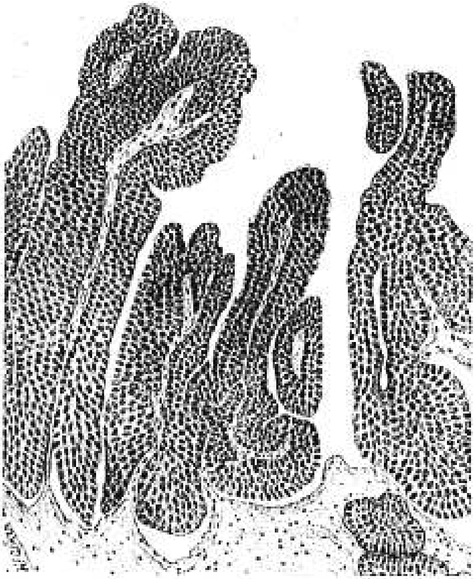

Fig. 7. Low power drawing of detail of same at point marked by arrow, showing regularity of epithelium and sharp line of demarcation between it and connective tissue stroma. The mitoses which were strikingly numerous are not shown.

What light does the clinical history of these cases after operation throw on this question?

In Case XX, eighteen months after the operation, death resulted from another disease without recurrence of bladder symptoms. In Case XXI, there have been no signs of a recurrence in the 8 years which have elapsed since the operation. In Case XXVI, there was a recurrence and a second operation, 18 months after the first, with death from the disease 2 months later. The histology of the recurrent growth will be considered under another heading. In Case XXXV, there were no bladder symptoms for 4 months after operation. No news since.*

Clinically then, one case (No. XXI) seems to have been proved benign. Another (Case XX) also probably benign. One case (No. XXVI), to be further considered later, may have been malignant from the first, but it is not necessarily so, and one (No. XXXV) still doubtful.

In 4 cases (Nos. XXIX, XXX, XXXIII, and XXXVII) the specimens removed contained portions of the bladder-wall including muscularis; careful examination of these failed to reveal evidences of epithelial infiltration in any. These specimens were of a similar nature to those already described; the first 3 of them, however, showed a greater proliferation of epithelium and a less typical arrangement, in fact a more malignant aspect, than any in the first group.

Case XXIX.—A papillomatous tumor the size of the end of a finger was removed from the bladder with the cautery, including a margin of healthy mucous membrane and a considerable extent of bladder-wall, including the muscularis. The tumor was incrusted with urinary salts. Doubtless owing in part to the escharotic effect of the cautery, and also on account of the necessary removal of the incrusted portions, the specimen was rather imperfect and confusing. A main stalk of considerable thickness could be made out, from which there were very fine lateral offshoots, covered with an extremely thick layer of epithelium. The epithelial cells were quite variable in size and shape, and showed in places a very irregular or atypical arrangement. There were occasional mitoses. The line of demarcation was not everywhere sharp between the epithelium and connective tissue of the stalk. There was marked round cell infiltration of the stalk. The bladder wall itself showed no epithelial infiltration.

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* This patient reëntered the hospital Feb. 5, 1906, with history of slight hæmaturia for 4 months. I did a suprapubic cystotomy and removed the prostate which was regarded as suspicious of malignant disease; there was no sign of a recurrence of the papilloma. Microspical examination of the prostate showed simple hypoertrophy. The patient is now convalescing.

Case XXX.—Section of a papillary growth 2x3 cm., with a portion of the base and muscularis of bladder-wall; there were a number of long, slender connective-tissue stalks covered with an exceedingly thick layer of epithelial cells. The villous processes in places were fused. The arrangement of the epithelial cells varied considerably in different parts of the growth, being in places quite typical, in others quite atypical. A number of mitoses were observed. The line of demarcation was not sharp; no epithelial infiltration of bladder-wall. There was an opportunity to examine the bladder two days later at autopsy in this case. A partial prostatectomy for adenoma of the prostate had been done at the same time that the papilloma was removed. The bladder was found to contain much clotted blood, with hemorrhagic infiltration of the tissues about the bladder. On the mucosa of the posterior bladder-wall there was a small shaggy mass with a short pedicle. The bladder wall at the site of removal of papilloma showed some thickening. Microscopic examination, however, according to the autopsy report, showed no evidence of carcinoma. This section could not afterwards be positively identified. The section of the small papilloma, found at autopsy, showed a papillary excrescence not larger than a pea, which was partly denuded of epithelium. The epithelium where it existed was disposed in few layers. Lying on the connective-tissue stroma just below the surface and in places communicating with the surface, were clumps of epithelial cells, some of which contained open spaces in the centre, giving to them a glandular appearance. There was no epithelial infiltration of the bladder-wall at the base of the tumor. The section corresponded closely to what Zuckerkandl has described and pictured as cystic papilloma.

Case XXXIII.—The specimen consisted of a pedunculated growth, 6 cm. in greatest diameter, which was removed from the bladder together with a considerable extent of underlying bladder-wall, including its muscularis. Microscopically the growth consisted of a number of long, slender stalks which were extremely vascular, radiating outwards from a circumscribed pedicle. These stalks were clothed with an epithelial covering of great thickness which consisted of large epithelial cells, varying considerably in size and arrangement.

In places the cells were packed together very closely, neighboring villi becoming fused and the papillary structure lost. In other places the arrangement was quite typical. Mitoses were rare. Line of demarcation between epithelium and connective tissue fairly sharp. There were evidences of intense inflammation of the bladder-wall, with round-cell infiltration. Absolutely no epithelial infiltration. The specimen is very like that in Case XXX.

CASE XXXVII.—In this case two tumors were removed from the bladder, one the size of a pigeon's egg on the right margin of the trigonum, and another smaller growth, size of a large pea, on the posterior wall above trigonum.

The larger section showed a papillary tumor with its pedicle but without bladder wall. (Fig. 2.) The stalk was comparatively coarse and contained muscle-fibres. The epithelium, less thick than in many of the preceding specimens, was composed of small, strikingly uniform, cylindrical cells, sharply marked off from the connective-tissue stroma. No mitoses were observed. The smaller specimen was of the same character, showing a good portion of the bladder wall without infiltration. Serial sections were made of both these specimens, but beyond demonstrating the fact that masses of epithelial cells, apparently enclosed in a connective-tissue stroma really were a part of the surface epithelium, showed nothing.

Clinically, in Case XXIX, there is perfect health 2 years and 2 months later. Case XXX has no clinical after-history; the histological evidence of benignity of the growth, is, however, quite complete.

In Case XXXIII there is perfect health one year later. Case XXXVII is too recent to be considered.

It would be premature to draw conclusions from these histories, but it may be said that, as yet, the histological findings have not been belied by the clinical data.

In 3 cases (Nos. XXXVIII, XXXIX, XLI) the specimens were obtained at autopsy, and cut together with a portion of the bladder-wall to which they were attached. In these cases an excellent opportunity was afforded to examine the whole thickness of the bladder-wall directly below the stalk of the tumor, but here, too, careful search failed to show the slightest evidence of epithelial infiltration in the submucosa or muscularis in any of them. Serial sections were not made.

CASE XXXVIII.—This specimen was a coarsely, papillary growth, about 2 cm. x3 cm., with a short stalk springing from the submucosa of the der-wall, containing large-sized blood-vessels. There was an intense inflammatory condition of both tumor and bladder-wall, evidenced by infiltration with leucocytes and necrosis. This considerably obscured the histology of the growth. The surface epithelium was mostly denuded; in one place only there were strips of a many-layered epithelium upon a connective-tissue stalk, forming a typical papillary process. The pedicle of the tumor, even close to its base, enclosed large masses of large variable-sized cells, some with several nuclei, which were regarded as atypical epithelial cells. There was no epithelial invasion of the bladder-wall itself.

CASE XXXIX.—The specimen was that of a villous tumor, 2x3 cm., the smaller of 2 similar growths, arising by a number of separate fine stalks from the submucosa of the bladder-wall. Viewed with a hand lens, the growth resembled a jungle of long grass. The long slender stalks, which showed but little branching, were covered with a comparatively narrow layer of cylindrical or spindle-shaped epithelial cells. Towards their ends the stalks were bare, the epithelium being stripped off and lying around loose, mostly at the bases of the stalks. Mitoses were rare. Many plasma cells were found in the connective-tissue stalks. There was no epithelial infiltration of the bladder-wall.

CASE XLI.—This specimen showed a delicate villous growth of small size, 1½x1½ cm., arising from the submucosa of the bladder-wall by a bunch of separate connective-tissue stalks. These stalks were long and slender, with but few branches, and were mostly stripped of epithelium, the epithelial cells lying loose in confused masses between the bases of the villi. These cells were cylindrical and spindle-shaped and varied considerably. There was absolutely no epithelial infiltration of the bladder wall. (Fig. 3.)

Summary.—A recapitulation of this analysis of the 11 cases regarded as papillomata may be stated as follows:

Four were demonstrated by complete histological examination of the base and bladder-wall to be benign. Cases XXX, XXXVIII, XXXIX, and XLI.

Three may be considered benign as far as a histological examination of a portion of the bladder-wall goes. Cases XXIX, XXXIII, XXXVII.

Of the 4 remaining cases which were histologically doubtful, one case (No. XXI) may be reasonably considered to have been benign in the light of the subsequent clinical history; probably also Case XX. One case (No. XXVI) which recurred in a malignant form may have been such from the start, though not necessarily. One case (No. XXXV) is still doubtful.

Number, Size, Situation, and Form.—In 7 of the 11 cases of papillomata the tumors were single; in each of the other 4 cases there were 2 tumors. There were no cases in this series with large numbers of papillomata,—papillomatosis.

The situation was not always exactly stated. The favorite site seemed to be at the base of the bladder near the ureteral openings. Where 2 tumors existed, the larger one was usually at the base of the bladder and the smaller on the posterior wall, at a point which would be in contact with the other when the viscus was empty. This was quite striking in Cases XXX and XXXVII, and seems to corroborate the theory of propagation by contact, which Albarran states is an indisputable fact.

In size the papillomata varied from one which was described in situ as being somewhat smaller than a lemon, which was the largest, to one the size of a small pea, the smallest.

As to form, there were two excellent specimens of the villous papillomata in Cases XXXIX and XLI; 6 were of the commoner, lobulated, or cauliflower type (Nos. XX, XXI, XXVI, XXXV, and XXXVII). The 3 remaining cases represented intermediate forms.

Cases of Carcinoma.—The specimens in the 6 cases regarded as carcinoma while affording sufficient histological data for a diagnosis, were not sufficient either in number or completeness to allow of a differentiation of varieties.

One specimen was obtained at autopsy, the other 5 at operations. The latter were removed piecemeal, so that they were necessarily fragmentary and incomplete. Only one of them showed the muscularis of the bladder-wall. In the other 4 specimens the question of infiltration, as far as the microscope was concerned, remained undetermined. It has been stated that infiltration of the bladder-wall is the distinctive mark of a papillary carcinoma of the bladder, and such it is in differentiating it from a papilloma; but where the structure is not of a papillary nature the diagnosis can be adequately made from the type and arrangement of the epithelium and its relation to the connective tissue, without reference to the bladder-wall.

A brief description of these specimens follows:

CASE XXIV.[1]—A sessile, friable tumor with a base the diameter of a silver dollar was removed by morcellement from the floor of the bladder. Sections of the fragments showed on the surface a few connective-tissue processes covered with epithelium, which were suggestive of a papillary structure, and a loose, columnar arrangement of epithelial cells in the connective tissue of what was regarded as the submucosa.

CASE XXVII.—The projecting portions of a hard mass, involving the base and posterior wall of the bladder, were removed by morcellement. The specimen on section showed masses of large atypical epithelial cells invading a stroma of connective tissue. No mucosa or muscularis of bladder-wall could be recognized.

CASE XXXI.—A "papillomatous" tumor of large size was removed from the anterior wall and base of the bladder. A section of a fragment of the growth showed in places an arrangement of the epithelium and connective-tissue stroma suggesting villi which had become fused; in other places the arrangement was of an alveolar structure. The cells were very large and flat, of squamous type. No part of the bladder-wall could be recognized as such, in the section. There were many cell inclusions in this specimen.

Six months later a secondary operation showed the base of the bladder completely studded with hard nodules, with considerable induration of the bladder-wall. Section of one of these nodules which was curetted off, showed solid masses of epithelial cells of smaller size than in the preceding growth, separated by fine, fibrous trabeculæ.

CASE XXXII.—A portion only of a mass involving the right side of the bladder was removed. On section it showed solid masses of large epithelial cells infiltrating between the bundles of muscular fibres of the bladder-wall.

CASE XXXIV.—At operation the bladder was seen to be covered with "villous-looking nodules," which were easily separated from the bladder-wall. The latter was diffusely infiltrated and the urethral orifice was surrounded by a growth which was scraped off. Section of a fragment showed masses of small epithelial cells separated by a fine vascular connective-tissue stroma. No "villi" were to be seen, nor could any portion of the bladder-wall be identified.

CASE XL.—In this case the tumor was found at autopsy. An abstract of the report follows: In the bladder an irregularly ovoid, fairly smooth tumor, about 2¾ cm. in greatest diameter, with short pedicle, situated near the beginning of prostatic urethra, was found. The mucous membrane of the neck of the bladder and trigonum was generally beset with numerous small, whitish, nodules. The prostate was enlarged. Sections of the tumor showed groups and columns of atypical epithelial cells in places forming more or less perfect tubular structures, arranged in a dense, fibrous-tissue stroma. A section of the prostate showed increase in the interstitial connective tissue and dilatation of the tubules with atrophy of their epithelium, a few columns and masses of carcinomatous cells were present in the lymph-spaces. There were metastases in the retroperitoneal lymph-nodes. The growth was regarded as an adeno-carcinoma, primary in the bladder.

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[1] This case has been reported by Dr. F. B. Harrington. Boston Med. & Surg. Jour., May 29, 1902.

Summary.—These 6 cases of carcinoma may be summed up as follows:

In Case XL, an adeno-carcinoma, which is a rare form of primary cancer of the bladder, the possibility that the original focus of disease was in the prostate cannot be positively denied.

In Case XXXII, an alveolar carcinoma, infiltrating the bladder-wall, the diagnosis is unassailable.

In Case XXIV, there was fairly satisfactory evidence of infiltration of the submucosa of the bladder-wall.

In the other 3 cases, microscopic evidence of infiltration of the bladder-wall was lacking; there was, however, macroscopic evidence of it at the time of operation. In all of the specimens the histological structure of groups of atypical epithelial cells enclosed in a connective-tissue stroma was sufficiently convincing; 2 cases (Nos. XXIV and XXXI) showed slight evidences of villi in places, sufficient to suggest papillary carcinoma.

The after-histories of these cases gives further proof of their malignancy, if any were needed.

In Case XXIV death resulted 6 months after the operation, the disease having returned with great loss of blood.

In Cases XXVII, XXXI, XXXII, and XXXIV, death from the disease resulted in from 2 weeks to 6 months after operation. In no case was there an autopsy.

Malignant Degeneration of a Benign Papilloma.—There has been much discussion upon this important subject, the weight of authority seeming to favor the possibility of such a change. Civiale first advanced the view that a benign papilloma of the bladder, called at that period fungus, might take on a cancerous change. This view is shared by Küster, Thompson, Orth, Von Antal, Ziegler, Albarran, Zuckerkandl and many others.

On the other hand, Rauschenbusch does not believe in this transition, and Lubarsch holds that it is not proven. Nitze, in his vast experience, has never observed a case in which a tumor of the bladder, removed at a second operation, showed a different structure from the original.

The subject being of much practical importance, it seems worth while to examine briefly the evidence.

In the first place, there is the analogy of authenticated cases of papilloma of the larynx becoming cancerous. This has been shown by Semon to be much rarer than was generally believed. He collected statistics of 10,774 cases of benign tumors of the larynx, in only 5 of which did he find the evidence of carcinomatous change incontrovertible. The scarcity of these cases is explained by Wendel on the ground that papilloma of the larynx, unlike papilloma of the bladder, occurs mostly at an age when there is but slight tendency to cancer.

Secondly, clinical evidence seems to support the theory, for how else are cases to be explained, of which a number have been reported by Fenwick and others, where there have been symptoms of painless hæmaturia for 20 years or more, and at operation papillary tumors have been removed, showing but limited epithelial infiltration of their bases? It does not seem reasonable to suppose that such cases could have been malignant from the start, when symptoms have been so mild and the progress of the lesion so slow.

Thirdly, there is a considerable accumulation of histological evidence by different observers. Orth states that he has observed a bladder in which near a large, unmistakably cancerous, papillary growth, smaller papillary tumors were present, in which nothing of a cancerous nature was to be found. A large number of similar observations are recorded in the literature.

Zuckerkandl recognizes two modes of cancerous transformation of a simple papilloma. In one he describes the process as beginning in the tumor itself. In this form the epithelial cells in places lose their regular form and arrangement; they become packed together in dense masses, numerous mitoses attest their rapid growth, and as a result of this epithelial proliferation, the line of demarcation between epithelium and stroma becomes less sharp, and in places groups of epithelial cells will be seen breaking into the connective-tissue spaces. In more advanced stages the papillary processes become fused and unrecognizable, only a sparse stroma with blood-vessels remaining of the original framework.

In the second form, the tumor itself remains anatomically benign in appearance, while deep in the underlying bladder-wall small metastatic masses of epithelial cells attest the malignancy of the growth. This form is illustrated by a reproduction of an actual specimen of a villous papilloma of extremely benign appearance, the exquisite malignancy of which is, however, shown by the presence of a small epithelial thrombus in the midst of the muscular coat of the bladder-wall. The first form of transformation is also illustrated by specimens.

Noteworthy cases similar to these have been reported by Colley, Schuchardt, Wendel, and others.

There is only one case in this series which can properly be considered under this heading:

CASE XXVI.—After 3½ years of intermittent hæmaturia a papillary tumor was removed from the bladder by operation. This growth has already been described among the papillomata. (Figs. 6 and 7.)

There was a recurrence of symptoms and a second operation one year and six months later, with death from the disease two months after the second operation. At this second operation the bladder was found to be filled with large soft masses of cauliflower appearance, which were extirpated with cutting forceps. The largest of these masses removed was 3 cm. in diameter. The only specimen preserved showed on section 4 papillary stalks arising from a connective-tissue base. No portion of the bladder-wall could be identified. The connective-tissue stalks were comparatively narrow, quite vascular, branched freely, and were covered with a very thick layer of epithelial cells. These cells varied considerably in size, and were packed together without definite arrangement, so that in places adjoining villi appeared fused together, producing an appearance not unlike alveolar cancer. In other places the papillary structure was quite regular. Mitoses were numerous. Everywhere the line of demarcation between epithelium and connective tissue was indistinct. The two tissues shaded insensibly into each other. Within a large blood-vessel of one of the stalks there was a group of epithelial cells; this was interpreted as an illusion, the result of the direction of the section, and not a real epithelial thrombus. Lying in the blood about the specimen both at the surface and at the edge of the connective-tissue base, there were small clumps of epithelial cells which were regarded as probably broken from the villi. There were, however, two clumps of epithelial cells which lay directly within the connective tissue of the base, not upon it, or at its edge, which could not but be regarded as evidence of infiltration. This fact, together with the macroscopic evidence of infiltration of the bladder-wall, makes it clear that the growth at the time of the second operation was a papillary carcinoma. (Fig. 8 and 9.)

This case is cited as a suggestive one; it cannot be claimed to be convincing, since the original specimen contained no bladder wall and therefore could not be proved to be benign.

SYMPTOMS AND COURSE OF THE DISEASE.

Hæmaturia is the cardinal symptom of tumor of the bladder; it is intermittent, at least at first, usually painless, except in malignant cases, unassociated with rest or motion, and unaffected by any therapeutic measure.

Of the 41 cases studied, hæmaturia was noted in 40, the only exception being Case XVIII, a myoma. In 20 cases it was the first symptom. In benign cases the bleeding may persist for years without other symptoms. The longest period noted among these cases was in No. V, in which case there had been intermittent hæmaturia for 16 years.

Sooner or later, however, a train of secondary symptoms is sure to arrive, due to infection of the urinary tract (cystitis, pyelitis, pyelo-nephritis, etc.,) or to mechanical blocking of the inflow or outflow of urine resulting in hydro or pyonephrosis or retention. The cases with symptoms of cystitis have already been enumerated. Retention was very common. Hydronephrosis was noted three times. Cases IV, XVII, and XXXVIII.

Incrustation of the tumor with urinary salts is a frequent occurrence and has already been fully considered. Necrosis

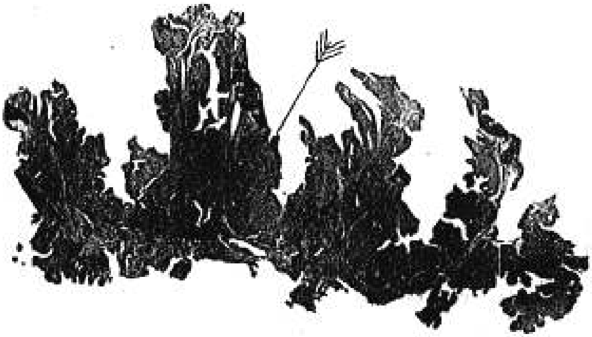

Fig. 8. Section of a fragment of recurrent papillary growth removed at second operation in (Case XXVI) x 5 diameters. No bladder wall is shown.

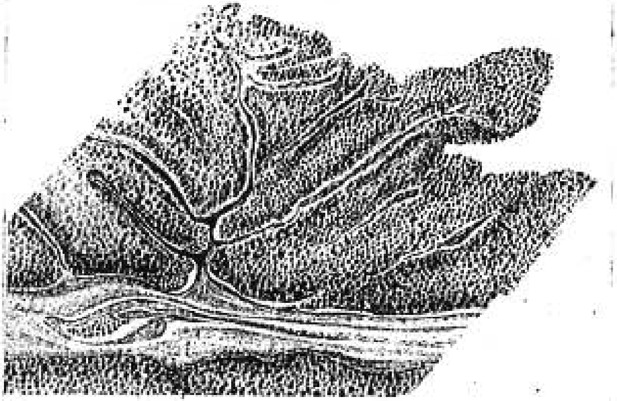

Fig. 9. Low-power drawing of detail of same at point marked by arrow in Fig. 8. The relative increase in epithelium, and the atypical character and arrangement of the cells, also the fusion of the villous processes contrasts markedly with Fig. 7.

and ulceration are more common in malignant cases. Perforation into the intestines or peritoneal cavity may even occur. It was not noted in any of these cases.

In general the course of a malignant tumor is much the same as in a benign, only more rapid. Cancer of the bladder, however, is considered to be of comparatively slow growth, setting up metastases late. There is usually more pain than in benign cases and, after ulceration has set in, the condition of the patient becomes truly pitiable.

DIAGNOSIS.

The value of cystoscopy in making the diagnosis of this condition cannot be overestimated. Data as to the size, situation, character, and number of growths, also as to the advisability of operation can be obtained by this means only.

The method is applicable to all cases with the 3 following exceptions: (1) where the urethra is impassable to the cystoscope; (2) where the hemorrhage is profuse and persistent; (3) where the growth on account of its size or position prevents the necessary manipulation of the instrument. The first obstacle can usually be overcome by appropriate methods of dilatation, the second by appropriate irrigation, or by the selection of a favorable opportunity, and the last is very unusual.

The method was employed in nearly all the recent cases in this series, and I think it might have been used with benefit in all of them. The time-honored methods of examination in all vesical diseases, such as examination of the urine, especially for villous fragments, rectal examination, etc., are also of value in making the diagnosis, and should not of course be neglected.

PROGNOSIS.

Albarran says "En clinique, ce qu'il faut dire, c'est que toute vesicale est maligne on peut le devenir."

Every tumor of the bladder unless removed will in time certainly lead to a fatal termination, either from hemorrhage, or as the result of the secondary changes already mentioned. Alleged cures by spontaneous extrusion of the growth through the urethra have been reported, but are too rare to substantially affect the truth of the preceding statement.

The clinical malignancy of the anatomically benign bladder-tumors could not be better illustrated than in Cases XXXIX and XLI.

CASE XXXIX.—A laborer, 60 years of age, was brought to the accident department of the hospital, December 22, 1900, with a history of having passed blood with his urine for 6 months. Three weeks ago the hæmaturia became constant. One week ago he took to his bed and has failed rapidly since.

He was profoundly anæmic, and nearly moribund when brought to the hospital. In spite of irrigations of the bladder with various styptics, the bleeding continued, and he died on the third day after entrance.

Autopsy revealed, as the source of hemorrhage, two pedunculated tumors, the larger 4x5½x1½ cm., about 2 cm. apart, springing from the mucosa of the bladder-wall just above the left ureteral orifice. One of these specimens was preserved and has already been described. There was no evidence either macroscopical or microscopical of epithelial infiltration of the bladder-wall.

CASE XLI.—A man fifty-five years old, entered the medical department of the hospital June 1, 1901, with the following history: An attack of hæmaturia 1½ years ago; at this time there was some pain referred to the penis. One year later there was another severe attack. For the last three weeks he has been passing blood and clots constantly. Has had heart trouble for years.

The bleeding continued, uninfluenced by various internal remedies and he died June 7. At autopsy, atheromatous endocarditis of the mitral valves was found, and fibrous endocarditis of the tricuspid valve with hypertrophy and dilatation of the heart. The bladder contained much clotted blood and showed on its posterior wall a small villous papilloma which has already been described. (See Fig. 3.) Other organs were not remarkable.

The severity of the cardiac lesions in this case undoubtedly explains why surgery was not resorted to.

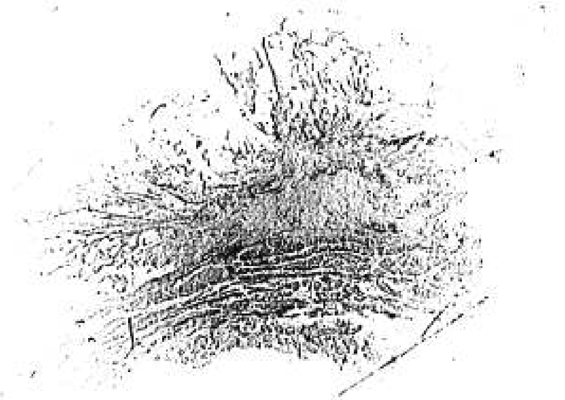

Fig. 3. Section of a villous papilloma x 6 diameters, anatomically benign, clinically malignant (Case XLI).

TREATMENT.

The only effective treatment of tumors of the bladder is operative removal. In malignant cases palliative measures may be advisable.

The treatment was operative in 37 of the cases here reported. In no case was an attempt made to radically remove an infiltrating cancer of the bladder-wall. Palliative measures, such as curettage, cauterization, and partial removal, were resorted to for symptomatic reasons in such cases.

Pedunculated tumors were removed with or without portions of the underlying bladder-wall, as the case might be.

Suprapubic cystotomy was done primarily in 28 cases, perineal cystotomy in 4, vaginal cystotomy in one; in 4 female cases the tumors were reached by dilatation of the urethra.

In 4 cases secondary suprapubic operations were done for recurrences. In one case the first operation at the hospital was for recurrence.

Results of Operation.—Of the 37 cases of all kinds, benign and malignant, favorable and unfavorable which came to operation, 9 resulted fatally within one month, or while still in the hospital, giving a mortality of slightly under 25 per cent. which can be ascribed to the operation.

Of the 28 patients who survived the operation and were discharged from the hospital, 26 have been traced; 14 (54 cent.) of these are known to have died of the disease; 12 of them died within 18 months of the operation.

In the 2 cases which survived a longer time, secondary operations were done for recurrent growths. In one of these cases, life was prolonged for 5 years after the first operation; 3 suprapubic cystotomies and several tappings of a hydronephrotic kidney having been done altogether. (Case XVII.)

Four patients (15 per cent.) have died of other diseases, without recurrence of the bladder-tumors, so far as could be learned.

In Case I, the cause of death was given as " renal calculi," 13 years after the removal of a bladder-tumor, of which there was no microscopical report.

In Case V, cause of death was typhoid fever 9 years after the removal of a papillary epithelial growth.

In Case IX, pulmonary tuberculosis was the cause of death 3 years after the removal of a bladder-tumor, of which there was no microscopical report.

In Case XX "shock" (cerebral hemorrhage) was given as the cause of death, 1 year and 6 months after the removal of a papilloma.

Seven patients (27 per cent.) were living and well at the time this investigation was made; 2 of these (Nos. XXXVI, a case of fibro-myo-sarcoma, and XXXVII, a case of papilloma) are too recent to count. One patient (No. XIV), a case in which there was no microscopical report of the tumor, was well for ten years after the operation.

Four patients (Cases XXI, XXIX, XXXIII, and XXXV, in which the tumors were papillomata), are living and well, respectively, 8 years, 2 years, 1 year and ½ year after the operation.

One patient (No. XVIII), a case of myoma, was in good health 2 years after the operation, but has not been heard from during the last 8 years.

It is impossible to fix upon any definite postoperative period of immunity as establishing a cure. Therefore, the word will be avoided in summing up the favorable results, which may be stated as follows:

Twelve patients (46 per cent.), including those who died of other diseases, have had no recurrence so far as known; 9 of these are known to have survived the operation one year; 7 survived the operation two years; 5 survived the operation 8 years; 3 of these dying of other diseases, leaving 2 patients (Nos. XIV and XXI), still living and well, respectively 8 and 10 years after operation.

The end results of the cases in which the histological character of the growths was personally studied, have already been incidentally mentioned.

The 5 cases of carcinoma which were operated upon, all resulted fatally within 6 months of the operation. In none of these cases was the operation radical.

Of the 8 cases of papillomata which were operated upon, there was:

One (Case XXX) in which death was the direct result of the operation.

One (Case XX) in which death resulted 18 months after the operation from another disease without recurrence.

One (Case XXVI) in which recurrence in the form of carcinoma took place, with death 2 months after a second operation.

In the other 5 cases (XXI, XXIX, XXXIII, XXXV, and XXXVII) the patients are still living and well.

Recurrence.—The cases in which recurrence occurred have already been detailed. It is the rule in cases of carcinoma and sarcoma, and common in papilloma. It is doubtful if the word can be properly applied in all cases of subsequent growths of the latter type. There are numerous instances where papillomata reappear in the bladder after removal, not at their previous sites but in other parts of the bladder-wall. In such cases there seems to be a predisposition or tendency towards the formation of papillary growths, which naturally is not affected by the mere removal of any one growth.

As a rule, rapidly and repeatedly-recurring tumors are malignant in the end if not from the beginning. *Vide* Case XVII of Table. That every recurrent papillary growth is malignant is not true, as is shown by the following case:

CASE XXI.—A man, aged 55 years, entered the hospital July 16, 1897, with the history that 7 years before he began to have more or less trouble in passing urine, with frequency at night.

There was a gradual onset of hæmaturia. Two years later he was operated on by Dr. Cabot in private, and a tumor was removed from the bladder by suprapubic cystotomy. He got along very well for three years after this, during which time it had been his custom to pass a catheter upon himself every other day. Then symptoms as before operation gradually returned. A suprapubic cystotomy was done by Dr. Cabot at the hospital. Two small pedunculated growths about the circumference of dimes were removed, and their bases cauterized. One of these was situated near the right ureteral orifice, the other to the right and behind the urethral orifice. The record stated that the latter was about on the site of the previous tumor.

The patient made an uneventful recovery and was seen by me on May 16, 1905, nearly 8 years after the second operation, when he reported his health to be excellent, without urinary symptoms of any kind. The urine was examined at this time and found to be normal in every way.

The two specimens in this case were alike. One of them has already been described. (See Figs. 4 and 5.)

CONCLUSIONS.

From this clinical and histological study of tumors of the bladder the following conclusions may be drawn:

1. Stone in the bladder is not an etiological factor of importance in the causation of these tumors.

2. The condition of the underlying bladder-wall in regard to epithelial infiltration, is the most satisfactory and reliable guide in the determination of the benign or malignant character of papillary epithelial tumors of the bladder.

3. If the foregoing condition is accepted as the differential test of these growths then will the benign forms commonly called papillomata, be found to at least equal if not outnumber the malignant, the papillary carcinomata.

4. Recurrent epithelial tumors are not necessarily malignant.

5. Papillary tumors of the bladder, proved to be histologically benign, may rapidly lead to a fatal result if let alone.

6. Surgical intervention at the proper time in the case of pedunculated papillary tumors of the bladder offers a very fair chance of long immunity, if not of permanent cure.

7. The method of surgical intervention to be preferred in these cases, is excision of the tumor in toto, with a margin of bladder-wall at its base, including mucosa, submucosa, and muscularis in part; the section need not penetrate the entire thickness of the wall. In this way, a beginning epithelial infiltration of the base if present, may be circumvented; or if it is not present, the knowledge of the fact is of great value in the important matters of diagnosis and prognosis. The defect in the bladder-wall should be closed with sutures, which will at the same time control hemorrhage. The gravity of the operation is not appreciably increased by this procedure.

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TABLE OF OPERATED CASES.

Case and Reference.	Date.	Age.	Sex.	Clinical Notes.	Operation.	Operator.	Nature of Tumor.	Immediate Result.	Ultimate Result.
I S.T.E.	Aug. 4, 1877	45	F.	Frequent and painful micturition 2 years. Hæmaturia 2 mos. Two previous plastic operations on vagina	Dilatation of urethra. Digital removal of bladder tumor	Dr. J. C. Warren	Villous growth incrusted with urinary salts. No microscopical report	Operative recovery	Died 15 yrs. later of renal calculi. (Mass. Archives)
II M.R.	Nov. 1, 1883	53	M.	Hæmaturia 5 mos. Severe pain, pyuria, chills. Passed cauliflower-like pieces of tissue	Perineal cystotomy, villous growth removed with curette	Dr. C. B. Porter	Fragments of growth passed in urine examined and reported as villous cancer. No microscopical report of tumor itself	Operative recovery Discharged with perineal fistula	Died 3 mos. later of cancer of bladder
III W.S.P.	Jan. 8, 1885	42	M.	Painful and frequent micturition. Little blood at the end of urination for 4 weeks	Perineal cystotomy, fungus growth removed with curette	Dr. C. B. Porter	Large rough tumor. No microscopical report	Died 9 days after operation. *Autopsy*, cancer of bladder wall with sloughing. Interstitial nephritis	
IV F.G.	Dec. 21, 1885	73	F.	First noticed urine was thick and brown 8 mos. ago; 2 mos. ago hæmaturia began accompanied by pain and frequency	Vaginal cystotomy, tumor the size of two English walnuts attached to post part of floor of bladder removed with curette	Dr. A. T. Cabot	Epithelial tumor incrusted with urinary salts (W. F. W.)	Died 7 days after operation. *Autopsy*, gangrenous cystitis, hydronephrosis and pyelitis	
V L.J.D.	Sep. 27, 1886	34	M.	Intermittent hæmaturia for 16 yrs. Blood has been constant for past few mos., occasional pain, retention twice	Supra pubic cystotomy, white cretaceous growth scraped from bladder with curette	Dr. C. B. Porter	Exam. of fragments passed in urine after sounding showed the growth to be of a papillary epithelial nature. No microscopical report of the tumor itself	Operative recovery	Died 9 yrs. later of typhoid fever. (Mass. Archives)
VI J.J.R.	Sep. 28, 1887	59	M.	Intermittent hæmaturia for 16 mos. Pain in lower abdomen	Supra pubic cystotomy, sessile tumor removed, base cauterized.	Dr. M. H. Richardson	No microscopical report	Died in 6 days. *Autopsy* showed diphtheritic cystitis and cellulitis	
VII J.C.	April 19, 1889	52	M.	No venereal history. Symptoms of cystitis for 9 mos., blood in urinary sediment	Supra pubic cystotomy, bladder tumor curetted out	Dr. J. Homans	Friable new growth largely filling bladder. Microscopical report, *Epithelioma* (W. F. W.)	Died in 7 days. No autopsy	

VIII A.W.	Nov. 19, 1889	50	M.	No venereal history. Dull pain in loin, intermittent hæmaturia beginning 10 months ago following a fall, occasional retention from clots. Hæmaturia constant for 4 wks.	Supra pubic cystotomy, small tumor near rt. ureteral orifice curetted out	Dr. C. B. Porter	No microscopical report	Operative recovery	Died of carcinoma of bladder 1 yr. and 5 mos. after operation
IX M.M.	Jan 9, 1890	29	F.	Symptoms of cystitis following confinement 9 mos. previous. Hæmaturia for 8 mos.	Dilatation of urethra, tumor size of walnut at base of bladder curetted out	Dr. J. W. Elliot	No microscopical report	Operative recovery	Died 13 yrs. later of tuberculosis of lungs (Mass. Archives)
X A.E.S.	Jan. 14, 1892	51	F.	For 2 years has had urethral discharge, at times blood stained; 5 wks. ago portion of growth removed from urethra. Symptoms, frequency, pain and tenesmus	Growth involving urethra and ant. wall of vagina curetted, urethra dilated and papillomatous tumor of bladder curetted out	Dr. C. B. Porter	Microscopical report, *Infiltrating cancer* (W. F. W.)	Operative recovery	Died 8 mos. later of cancer of bladder
XI S.C.W.	Jan. 18, 1892	55	M.	No venereal; 20 yrs. ago had slight trouble in passing water for a few mos., no further trouble until 1 yr. ago when he first noticed clots of blood in urine. Intermittent hæmaturia since. Retention from clots	Perineal cystotomy, large papillomatous tumor attached to base of bladder removed with stone forceps	Dr. A. T. Cabot	No microscopical report	Operative recovery Developed insanity during convalescence	Died 1 yr. later with recurrence
XII E.S.	May 13, 1892	65	M.	Hæmaturia for 5 mos. Pain and frequency followed. Lost 50 lbs. in weight	Perineal cystotomy, tumor size of walnut curetted off bladder wall	Dr. J. Homans	No microscopical report	Operative recovery	Further history unknown
XIII J.G.	July 12, 1892	54	M.	Gonorrhœa 35 yrs. ago. Symptoms of cystitis began 8 wks. ago, 6 weeks ago began to pass blood.	Supra pubic cystotomy, tumor removed with curette, tumor was size of baby's hand above the ureteral orifice	Dr. A. T. Cabot	Microscopical report, *Cancer* (W. F. W.)	Operative recovery	Died 3 mos. later with recurrence
XIV J.H.	July 10, 1894	34	M.	Gonorrhœa 15 yrs. ago. Hæmaturia began 2 mos. ago following a fall. Constant bearing down pain	Supra pubic cystotomy, hard and dense tumor 2 in. by 1½ in., on floor of bladder removed with chain écraseur	Dr. S. J. Mixter	No microscopical report	Operative recovery	In perfect health Feb., 1905. Personally examined
XV J.E.B.	July 19, 1894	46	M.	In 1870 lateral perineal lithotomy. Frequency of micturition ever since. In 1889 supra pubic cystotomy by Dr. Cabot at M. G. H. "Pachydermia vesicae." Re-enters hospital with a broken-down supra pubic sinus and symptoms of severe cystitis with hæmaturia	Supra pubic sinus dilated, bladder explored, portion of a new growth removed with forceps	Dr. A. T. Cabot	Microscopical report, *Epidermoid cancer* (W. F. W.)	Gradually failed and died 1 month after operation. Autopsy showed cancer involving bladder wall, abdominal wall and retro-peritoneal glands	

TABLE OF OPERATED CASES—*Continued.*

Case and Reference.	Date.	Age.	Sex.	Clinical Notes.	Operation.	Operator.	Nature of Tumor.	Immediate Result.	Ultimate Result.
XVI G.C.F.	Dec. 22, 1894	61	M.	No venereal. Frequency for 7 mos. Hæmaturia 8 wks. Occasional stoppage. Pain for last 2 wks.	Supra pubic cystotomy, growth curetted from int. urethral orifice	Dr. C. B. Porter	Fragments obtained by washing bladder reported as papilloma. Microscopical report of masses removed at operation, *Cancer*, (W. F. W.)	Died 2 weeks later. No autopsy	
XVII * S.H.T.	Jan. 9, 1895	53	M.	No venereal. Frequency of micturition with scalding began 6 yrs. ago. Hæmaturia 1 year ago	No. 1—Supra pubic cystotomy, tumor size of Mandarin orange removed piecemeal from post. wall	Dr. S. J. Mixter	No microscopical report	Operative recovery	The hydronephrotic kidney refilled and was tapped several times subsequently. In March 1901, sound could not be made to enter bladder, which seemed filled with new growth. Patient died of the disease a few mos. later
	Re-entry, April 30, 1896			Relieved by operation for 1 yr. then hæmaturia recurred	No. 2—Supra pubic cystotomy, tumor size of orange on ant. wall removed with scissors and base cauterized	"	Microscopical report, cancer with slight infiltration of bladder wall (W. F. W.)	Operative recovery	
	Re-entry, June 23, 1897			Pain and hæmaturia recurred in 6 mos.	No. 3—Supra pubic cystotomy, papillomatous growth size of plum projecting from lower post. wall of bladder removed with curette		Microscopical report, Papillary cancer (W. F. W.)	Operative recovery	
	Re-entry, April 24, 1900			Pain and pressure in left side	No. 4—Cystic tumor in left hypochondrum tapped, ℥ cvii brownish fluid evacuated	"	....	Temporary relief	
XVIII M.V.B.M.	Nov. 12, 1895	57	M.	Stricture of urethra 15 yrs. ago; 9 yrs. ago renal colic, later passed some small stones, 1 yr. ago symptoms of cystitis began. In Feb., '95, litholapaxy at M. G. H. and again in August by Dr. Cabot in private. In Sept. a stone was washed out of bladder. In Nov. same symptoms recurred and he re-entered hospital	Supra pubic cystotomy, stone removed from post. prostatic pouch, two small hard projections incrusted with urinary salts removed from bladder wall	Dr. A. T. Cabot	Microscopical report, Myoma (W. F. W.)	Operative recovery	In good health 2 years after operation. Not heard from since

* This case has been reported by Dr. Mixter. Boston Medical and Surgical Journal, April 20, 1899.

XIX C.S.	Feb. 22, 1896	70	M.	No venereal. Pain and frequency 2 yrs, hæmaturia 8 months	Supra pubic cystotomy, large sessile tumor on right side of bladder curetted out	Dr. A. T. Cabot	Microscopical report, Flatcell cancer (W. F. W.)	Died in hospital 4 mos. later. Incomplete autopsy showed bladder extensively involved in growth	
XX S.B.	June 28, 1897	52	M.	Gonorrhœa 30 yrs. ago. Painless hæmaturia began 1½ yrs. ago. Later pain in left testicle and kidney	Supra pubic cystotomy, growth size of strawberry on post. wall above trigonum removed, base curetted	Dr. S. J. Mixter	Microscopical report, Papilloma. Impossible to say whether malignant or not (J. H. W.)	Operative recovery	Died 1 year and 6 months later of shock (cerebral hemorrhage) without recurrence of bladder symptoms
XXI E.S.	July 16, 1897	55	M.	No venereal; 7 years ago symptoms of frequency and afterwards hæmaturia began; 5 yrs. ago papilloma removed from bladder by Dr. A. T. Cabot in private; 2 yrs. ago symptoms recurred as before	Supra pubic cystotomy. two small tumors removed with forceps and their bases cauterized, one was situated to the outer side of the rt. ureteral orifice, the other behind uretral orifice about on the site of the previous tumor	Dr. A. T. Cabot	Microscopical report, *Papilloma*. Impossible to say whether or not malignant (J. H. W.)	Operative recovery	Personally examined in May, 1905, nearly 8 yrs. after second operation. Health perfect
XXII H.A.T.	Sep. 26, 1899	63	M.	No venereal. Frequency and hæmaturia for 6 mos. Occasional retention	Supra pubic cystotomy, growth on rt. side of bladder extending toward prostate curetted out, base cauterized	Dr. J. C. Warren	Microscopical report, *Cancer* (W. F. W.).	Operative recovery	Died 2 mos. later of recurrence
XXIII N.K.	May 13, 1900	26	F.	Symptoms of cystitis with hæmaturia for 2 yrs. following confinement. Passed several stones	No. 1—Dilatation of urethra, two small tumors, one on post. wall, one on left side, removed, bases curetted	Dr. J. W. Elliot	No microscopical report	Operative recovery	
	Re-entry, Dec. 1, 1900			Painful and bloody urination, returned soon after leaving hospital.	No. 2—Supra pubic cystotomy, deposit of calcareous matter on bladder wall curetted off, two small papillomatous masses removed	Dr. R. B. Greenough	No microscopical report	Operative recovery	Subsequent history unknown
XXIV J.P.K.	Aug. 20, 1900	49	M.	Hæmaturia began 10 wks. ago. Pain and frequency began soon after	Supra pubic cystotomy, sessile friable tumor with base size of silver dollar removed from base of bladder with prostatome	Dr. F. B. Harrington	Microscopical report, *Villous Carcinoma* (J. H. W.)	Operative recovery	Died in another hospital with recurrence 1 yr. and 6 mos. later
XXV L.V.	Oct. 29, 1900	69	M.	No venereal. Pain, frequency and hæmaturia began about 6 mos. ago	Supra pubic cystotomy, a soft sloughing pedunculated tumor at neck of bladder removed with curette	Dr. J. C. Warren	No microscopical report	Operative recovery	Died 3 mos. later of cancer of bladder

TABLE OF OPERATED CASES—*Continued.*

Case and Reference.	Date.	Age.	Sex.	Clinical Notes.	Operation.	Operator.	Nature of Tumor.	Immediate Result.	Ultimate Result.
XXVI F.H.D.	Dec. 31, 1900	58	M.	Gonorrhœa 38 yrs. ago. Hæmaturia began 1 yr. and 3 mos. ago. Intermittent since. Frequency during last month; 3 attacks of retention	Supra pubic cystotomy, soft papillary mass on left side of bladder removed with forceps, base cauterized	Dr. A. T. Cabot	Microscopical report, *Papillary cancer* (W. F. W.)	Operative recovery	
	Re-entry, July 2, 1902			Blood re-appeared in urine 6 months after operation and continued with frequency and and tenesmus	Supra pubic cystotomy, bladder filled with large soft cauliflower mass which was removed piecemeal with forceps	"	Microscopical report, *Papilloma* (C. C. S.).	Discharged from hospital with permanent bladder drainage	Died 2 mos. later of the disease
XXVII F.L.	June 6, 1901	53	F.	Frequency 10 mos. Hæmaturia 8 mos. Pain	Supra pubic cystotomy, hard irregular mass involving base and post. wall of bladder, projecting portions of growth removed, curetted and cauterized	Dr. F. B. Harrington	Microscopical report, *Mesothelial cancer* (W. F. W.)	Operative recovery	Died 6 mos. later of the disease
XXVIII S.S.	Mar. 11, 1903	58	M.	No venereal. Hæmaturia 10 mos. Pain in left back. Frequency of micturition for 6 months	Supra pubic cystotomy, a mass projecting into the right side of the bladder removed with prostatic forceps, the growth also extended into pelvis, no attempt was made to remove it	Dr. A. T. Cabot	Microscopical report, *Round cell sarcoma* (W. F. W.)	Discharged from hospital with permanent supra pubic drainage	Died 2 mos. later of the disease
XXIX T.A.B.	Mar. 17, 1903	59	M.	No venereal. Hæmaturia 3 months.	Supra pubic cystotomy, papillomatous growth to the left of prostate removed with a margin of normal mucus membrane with cautery	Dr. A. T. Cabot	Tumor size of end of finger incrusted with urinary salts. Microscopical report, Malignant Papilloma. No evidence of infiltration of bladder wall (W. F. W.)	Operative recovery	Letter of May, 1905, reports perfect health. No urinary symptoms of any kind
XXX W.H.	July 8, 1903	57	M.	No venereal. Intermittent hæmaturia for 4 yrs. Slight pain and frequency	Supra pubic cystotomy, papillomatous tumor size of egg removed from ant. wall on left, bladder wall sutured, 3d lobe of prostate found enlarged and removed with prostatome	Dr. W. M. Conant	Microscopical report, *Papilloma, probably malignant* (C. C. S.) Adenoma of prostate.	Died in 24 hours. *Autopsy* showed hemorrhage into bladder; on post. wall of bladder small papilloma found; examination of bladder wall showed no epithelial infiltration	

XXXI N.W.	Jan. 31, 1904	40	M.	Operated on for stone in the bladder at the age of 9. No further urinary symptoms until hæmaturia began 2½ yrs. ago. Intermittent since	No. 1—Supra pubic cystotomy, papillomatous tumor at base of ant. wall of bladder removed with prostatic forceps	Dr. A. T. Cabot	Microscopical report, *Epithelioma* (W. F. W.)	Operative recovery	
	Re-entry, Aug. 1, 1904			After leaving hospital improved at first, then old symptoms returned	No. 2—Supra pubic cystotomy, base of bladder studded with hard nodules, considerable induration of bladder wall, nodules removed with curette and cautery	Dr. W. M. Conant	Microscopical report, *Carcinoma* (C. C. S.).	Operative recovery	Died of the disease 2 mos. later
XXXII E.B.	Mar. 14, 1904	58	M.	No venereal; 1 yr. ago passed gravel, 6 weeks ago retention; 3 weeks ago pain and bleeding began	Supra pubic cystotomy, mass involving left side of bladder, portion of growth removed	Dr. M. H. Richardson	Microscopical report, cancer	Operative recovery	Died 3 mos. later of the disease
XXXIII S.S.R.	May 10, 1904	63	F.	Intermittent painless hæmaturia for 2½ yrs.	Supra pubic cystotomy, pedunculated papillary growth size of lemon on post. wall of bladder excised at base, defect in bladder wall sutured	Dr. J. W. Elliot	Growth 6 cm. diam., pedicle 1 cm. Microscopical report, *Malignant papilloma*. No evidence of infiltration of bladder wall. (W. F. W.)	Operative recovery	Letter of May, 1905, reports perfect health. No urinary symptoms
XXXIV E.B.	June 2, 1904	57	M.	Frequency 8 mos. Pain in back and hæmaturia 1 mo. Retention	Supra pubic cystotomy, bladder mm. covered with villous nodules, urethral orifice surrounded by a growth which was scraped off	Dr. S. J. Mixter	Nodular fragments from the bladder, the wall of which was diffusely infiltrated with a new growth. Microscopical exam., *Cancer* (W. F. W.)	Died in 2 weeks; septic absorption. No autopsy	
XXXV A.M.	Dec. 20, 1904	58	M.	No venereal. Hæmaturia began 2 yrs. ago with constant dull pain in flank. Frequency occurred later	Supra pubic cystotomy, pedunculated tumor size of strawberry just above rt. ureteral orifice removed with scissors, with small margin of mucous membrane, site of tumor cauterized	Dr. L. Davis	Coarsely papillary tumor size of horse chestnut. Microscopical exam., *Malignant papilloma* (W. F. W.)	Operative recovery	Supra pubic prostatectomy Feb. 17, 1906. No recurrence
XXXVI M.S.	April 27, 1905	16	M.	19 mos. ago hæmaturia began accompanied by great pain. Frequency of micturition later developed with nocturnal incontinence	Supra pubic cystotomy, a firm tumor size of orange arising by a thick short pedicle from the right side of internal meatus removed en morcellement, leaving a thick, ragged base which was cauterized, lower portion of tumor was incrusted with urinary salts	Dr. F. G. Balch	Microscopical report, *Filro-myo-sarcoma* (W. F. W.)	Operative recovery Discharged July 2 with small supra pubic fistula	Case too recent for data
XXXVII M.J.C.	Sep. 16, 1905	51	M.	Gonorrhœa many years ago; 2 years ago began to pass bloody urine without pain; 2 wks. ago retention	Supra pubic cystotomy, larger tumor removed from right edge of trigonum with scissors, site of tumor cauterized, smaller one on post. wall of bladder removed with a good margin, defect in bladder wall sutured	Dr. J. G. Mumford	Microscopical report, *Malignant papilloma* (W. F. W.)	Operative recovery Discharged from hospital Nov. 4, 1905, with granulating wound above pubes	Case too recent for data

TABLE OF UNOPERATED CASES OF TUMOR OF THE BLADDER FOUND AT AUTOPSY.

No.	Date	Age	Sex	Clinical Notes	Post-mortem Findings
XXXVIII Autopsy 87	April 15, 1897	70	Male	No venereal. Two years ago passed gravel. Five months ago began to have frequency of micturition. Hæmaturia began one month later and has been constant since, with much pain. Operation was deemed inadvisable on account of poor general condition. Patient slowly failed and died April 23, 1897.	"Papilloma of Bladder. Diphtheritic cystitis. Inflammatory infiltration of peri-vesical tissues. Sl. pyelo-nephrosis of left kidney. Sl. hydronephrosis of right kidney. Acute peritonitis. Acute degeneration of kidney. Infarction of kidney. Arterio-sclerosis with cardiac hypertrophy and dilatation. Emphysema. Hypostatic congestion and œdema of lungs."
XXXIX Autopsy 641	Dec. 22, 1900	60	Male	Brought to accident room in extremely weak and anæmic condition with history of having passed bloody urine for 6 months. Failed rapidly during last 3 weeks. In spite of washing the bladder with various styptic solutions, the hemorrhage continued and the patient died in 3 days.	"Papillomata of the bladder. Hemorrhage into bladder. General anæmia. Fatty degeneration of heart muscle. Concentric hypertrophy and dilatation of heart. Arterio-sclerosis of aorta and coronary arteries. Chronic atheromatous endocarditis of mitral valve with acute vegetations. Œdema of lungs. Cholelithiasis. Hyperplasia of spleen. Cysts of right kidney. Right hydrocele."
XL Autopsy 681	Feb. 25, 1901	64	Male	No venereal. Severe attacks of pain in region of left kidney for 20 years. Hæmaturia during last 2 months. An exploratory nephrotomy was done with negative result, and the bladder searched for stone without result. Patient died 4 days later with partial suppression of urine.	"Nephrotomy with hemorrhage into peri-nephric and retroperitoneal tissues. Adenocarcinoma of the neck of the bladder with metastasis in the retroperitoneal lymphatic glands. Senile degeneration of the kidneys. Adenoma of the prostate. Chronic interstitial prostatitis. Chronic pericholecystitis and perihepatitis. Œdema of lungs. Ecchymoses in the mucous membrane of the stomach. Defective closure of the foramen ovale of heart."
XLI Autopsy 710	June 8, 1901	55	Male	Heart trouble since childhood. Painless hæmaturia began 1½ years ago. For 3 weeks the bleeding was constant. Bleeding continued while in the hospital, with death at the end of a week. (Operation not undertaken presumably on account of heart.)	"Papilloma of Bladder with hemorrhage. General anæmia. Atheromatous endocarditis of the mitral and aortic valves. Fibrous endocarditis of the tricuspid valve. Hypertrophy and dilatation of the heart. Concretions in the prostate."